

What is claimed is:

1. A composition comprising a compound which binds to a receptor for "GLP-1", and a pharmaceutical carrier, said compound being present in an amount effective to enhance the sensitivity and response of pancreatic  $\beta$ -cells to changes in plasma glucose, as measured by the timing and amount of insulin secretions in response to increases in plasma glucose, in a human with impaired glucose tolerance.
2. The composition of claim 1 wherein the receptor-binding compound is selected from (a) a peptide which comprises the amino acid sequence of glucagon-like peptide-1, and (b) a variant peptide comprising an amino acid sequence that differs from the sequence of glucagon-like peptide-1 by one or more substitutions, deletions or insertions.
3. The composition of claim 2 wherein the receptor binding compound is glucagon-like peptide-1.
4. The compound of claim 2 wherein the receptor binding compound is glucagon-like peptide-1 (7-37) which has the sequence His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly (SEQ. ID NO:3).
5. The compound of claim 2 wherein the receptor binding compound is glucagon-like peptide-1 (7-36) amide which has the sequence His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg (NH<sub>2</sub>) (SEQ. ID NO:4).
6. The composition of claim 2 wherein the receptor binding compound is a variant peptide in which the combination of the substitutions, deletions and

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Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala  
Trp Leu Val Lys Gly Arg Gly (SEQ. ID NO:3).

14. The method of claim 11 wherein the receptor binding compound is  
5 glucagon-like peptide-1 (7-36) amide which has the sequence His Ala Glu Gly  
Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile  
Ala Trp Leu Val Lys Gly Arg (NH<sub>2</sub>) (SEQ. ID NO:4).

15. The method of claim 11 wherein the receptor binding compound is a  
10 variant peptide in which the combination of the substitutions, deletions and  
insertions in the amino acid sequence does not differ by more than ten amino  
acids from the amino acid sequence of glucagon-like peptide-1.

16. The method of claim 10 wherein the receptor binding compound is  
15 expressed by a polynucleotide.

17. The method of claim 10 wherein the receptor binding compound is an  
organic molecule having a molecular weight of not greater than about 5000.

18. The method of claim 10 wherein the step of administering is selected  
20 from the group consisting of intravenous, subcutaneous, intramuscular,  
interperitoneal, injected depot with sustained release, deep lung insufflation  
with sustained release, buccal or patch.

19. The method of claim 10, further comprising administering an agent that  
25 enhances the half-life *in vivo* of said receptor binding compound.

20. The method of claim 19 wherein the agent is administered concurrently  
with the composition.

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21. The method of claim 19 wherein the agent is covalently linked to the receptor binding compound.

22. The method of claim 18 wherein intravenous administration is in a dose  
5 range of from about 0.3 to about 2.0 pmol/kg per minute.

23. The method of claim 18 wherein continuous subcutaneous administration is in a dose range of from about 1.0 to about 20.0 pmol/kg per minute.

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24. A method for treating a human with impaired glucose tolerance, comprising: administering to the human a composition comprising a compound which binds to a receptor for glucagon-like peptide-1 and a pharmaceutical carrier, said composition containing an amount of said  
15 compound effective to retard or arrest the loss of plasma glucose control and the development of non-insulin dependent diabetes mellitus.

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25. The method of claim 24 wherein the receptor binding compound is selected from (a) a peptide which comprises the amino acid sequence of glucagon-like peptide-1, and (b) a variant peptide comprising an amino acid sequence that differs from the sequence of glucagon-like peptide-1 by one or more substitutions, deletions or insertions.

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26. The method of claim 25 wherein the receptor binding compound is glucagon-like peptide-1.

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27. The method of claim 25 wherein the receptor binding compound is glucagon-like peptide-1 (7-37) which has the sequence His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly (SEQ. ID NO:3).

28. The method of claim 25 wherein the receptor binding compound is glucagon-like peptide-1 (7-36) amide which has the sequence His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg (NH<sub>2</sub>) (SEQ. ID NO:4).

29. The method of claim 25 wherein the receptor binding compound is a variant peptide in which the combination of the substitutions, deletions and insertions in the amino acid sequence does not differ by more than five amino acids from the amino acid sequence of glucagon-like peptide-1.

30. The method of claim 24 wherein the receptor binding compound is expressed by a polynucleotide.

31. The method of claim 24 wherein the receptor binding compound is an organic molecule having a molecular weight of not greater than about 5000.

32. The method of claim 24 wherein the step of administering is selected from the group consisting of intravenous, subcutaneous, intramuscular, interperitoneal, injected depot with sustained release, deep lung insufflation with sustained release, buccal or patch.

33. The method of claim 32 wherein intravenous administration is in a dose range of from about 0.1 to about 10.0 pmol/kg per minute.

34. The method of claim 32 wherein continuous subcutaneous administration is in a dose range of from about 0.1 to about 75.0 pmol/kg per minute.

35. A method for treating an individual with impaired glucose tolerance comprising: administering to said individual a composition comprising a compound which binds to a receptor for glucagon-like peptide-1 and a

pharmaceutical carrier, wherein said composition contains an amount of said compound effective to improve entrainment of  $\beta$ -cell insulin secretory responses to exogenous glucose oscillations.

5 36. A method for treating an individual with impaired glucose tolerance comprising: administering to said individual a composition comprising a compound which binds to a receptor for glucagon-like peptide-1 and a pharmaceutical carrier, said composition containing an amount of said compound effective to enhance a normalization of insulin secretory patterns in  
10 impaired glucose tolerance.

37. A method for treating an individual with impaired glucose tolerance comprising: administering to said individual a compound which binds to a receptor for glucagon-like peptide-1 and a pharmaceutical carrier, said  
15 composition containing an amount of said compound effective to reduce plasma insulin levels in an individual with impaired glucose tolerance.

38. A method for treating an individual with impaired glucose tolerance comprising: administering to said individual a composition comprising a  
20 compound which binds to a receptor for glucagon-like peptide-1 and a pharmaceutical carrier, said composition containing an amount of said compound effective to reduce insulin resistance in an individual with impaired glucose tolerance.

39. A method for treating an individual whose symptoms indicate increased risk of a cardiovascular event comprising: administering to said individual a composition comprising a compound which binds to a receptor for glucagon-like peptide-1 and a pharmaceutical carrier, said composition containing an  
25 amount of said compound effective to enhance the regularity of insulin responses, and the amplitude thereof, in reaction to changes in plasma glucose,  
30 and to reduce plasma insulin levels.

40. A method for treating an individual whose symptoms indicate increased risk of a cerebrovascular event comprising: administering to said individual a composition comprising a compound which binds to a receptor for glucagon-like peptide-1 and a pharmaceutical carrier, said composition containing an amount of said compound effective to enhance the regularity of insulin responses, and the amplitude thereof, in reaction to changes in plasma glucose, and to reduce plasma insulin levels.

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